

A cross-sectional analysis of serum vitamin D and immunoglobulin E in allergic disorders

Vitamin D and IgE in allergic disorders

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Abstract

Aim: Allergic disorders constitute a major health problem in the modern world. Hypersensitivity to various allergens mediated by immunoglobulin E (IgE) forms the pathologic basis of allergies. The emerging role of vitamin D in immunity makes it a potential preventative and therapeutic agent against allergies. The present study explored the link between serum vitamin D and IgE levels in local patients with known allergies.

Material and Methods: Eighty subjects were recruited for this cross-sectional study and segregated into Group 1 (non-allergic control subjects, n=41) and Group 2 (allergic subjects, n=39). Complete blood count (CBC), serum IgE and serum vitamin D with its associated biochemical markers, including parathyroid hormone (PTH), calcium and phosphate were determined for comparison between the two groups. Basic demographic data, medical history and sun exposure duration were also recorded.

Results: IgE levels (Group 1, 87.13 IU/L \pm 57.66 vs. Group 2, 1542.54 IU/L \pm 1239.79; p=0.000) and eosinophil count (Group 1, 2.80% \pm 1.83 vs. Group 2, 4.61% \pm 4.19; p=0.014) were significantly higher in patients with allergies. No difference was observed between the groups in serum vitamin D levels and other markers. In patients with allergies, serum vitamin D was inversely related to serum IgE (r= -0.374, p= 0.019).

Discussion: High serum vitamin D is associated with low IgE levels in patients suffering from allergic conditions, suggesting a potential interplay between allergic mechanisms and vitamin D. Further studies are warranted to clarify the role of vitamin D in the pathogenesis and clinical management of allergic disorders.

Keywords

Allergy; Vitamin D; Immunity; Immunoglobulin E; Hypersensitivity

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Introduction

Allergic conditions constitute a major worldwide cause of chronic disability in individuals of all age groups and have a tremendous negative health economic impact. Allergic disorders have a complex etiology, with an almost equal contribution of genetic susceptibility and exposure to environmental factors [1]. In the last few decades, the prevalence of allergic conditions such as asthma, allergic rhinitis, atopic dermatitis, allergic conjunctivitis and food allergies has increased considerably [2-5]. With booming populations, growing urbanization and increasing westernization, South Asian countries have experienced a rise in allergic disorders due to a mix of environmental exposure and genetics due to high prevalence of consanguinity [6]. Immunoglobulin E (IgE) antibodies produced by the B-cells of the immune system lie at the heart of the hypersensitivity response seen in these allergic conditions. IgE, by binding to high-affinity IgE receptors present on the surface of basophils and mast cells, trigger degranulation and release of histamine and leukotrienes upon interaction with the allergens, which causes pronounced inflammatory responses leading to various allergic manifestations such as sneezing, bronchospasm, excessive nasal secretion, skin rashes along with itching, hyperemia, swelling and fever [7, 8].

Vitamin D is a fat-soluble vitamin obtained chiefly by dermal photobiogenesis that yields pro-vitamin D (cholecalciferol), which is subsequently activated into vitamin D (1,25-dihydroxy cholecalciferol) through hepatic and renal metabolic transformations [9]. Primarily involved in calcium homeostasis, recent evidence suggests a multifunctional activity of Vitamin D. It has been found to serve important roles in glucose metabolism, cardiovascular function, neuroprotection, endocrine control and immune regulation [10]. Vitamin D mediates immunity via a multitude of mechanisms including inhibition of the production of interleukins by T-cells and immunoglobulins by B-cells [11]. Vitamin D exerts immunomodulatory effects on allergen-induced hypersensitivity via activation of vitamin D receptor (VDR), which is expressed on B cells, T cells, regulatory T cells (Tregs), dendritic cells and macrophages [1]. Biochemical variations in vitamin D status alter the development and function of these immune cells, thereby modulating immune mediators like IgE and cytokines, and affecting the allergic response [12].

There are conflicting reports regarding the clinical role of vitamin D in allergic disorders, and loco-regional data are limited [6, 13, 14]. Vitamin D deficiency is quite common in the local population, and so are allergies. However, the existing data on the association between serum vitamin D and IgE levels are not clear [15]. The present study investigated the potential impact of vitamin D on IgE hypersensitivity in locally affected populace by ascertaining the correlation between serum vitamin D and IgE levels. Serum parathyroid hormone (PTH) levels were also determined due to its role in regulating vitamin D and mineral metabolism [16], along with serum calcium (Ca), serum phosphorus (P), complete blood count (CBC) and sun exposure for comparison with healthy non-allergic individuals.

Material and Methods

This analytical cross-sectional study was conducted from May 2020 to October 2020 in compliance with the ethical guidelines

as outlined in the Helsinki Declaration. Study approval was granted by the Research Committee, College of Pharmacy, University of Hafr Al-Batin. Considering a 20% incidence of allergic disorders, a total of 80 subjects between the ages of 15 to 65 years were recruited from Lahore, Pakistan out of the target population of 1.2 million people based on a 90% confidence level and $\pm 9.25\%$ margin of error. Subjects taking multivitamin and/or nutritional supplements or steroids for any condition were excluded. Subjects with known history of bone disorders, autoimmune conditions, renal failure and/or hepatic diseases were also excluded. Written informed consent was obtained from each study participant prior to recruitment. The participants were grouped into two groups: Group 1 (n=41) comprised of healthy persons without any known allergy, while Group 2 (n=39) included patients having diagnosed allergy. Detailed medical history and demographic data were obtained from all subjects to ensure fulfillment of inclusion and exclusion criteria. Personal data were kept completely anonymous. Venous blood (5 ml) was drawn and centrifuged at 3000 revolutions/minute for 10 minutes. Serum was separated and stored in aliquots at -20°C until analysis. Another 5 ml of blood was drawn in EDTA containing vacutainer tubes for complete blood count (CBC) including hemoglobin (Hb), hematocrit and blood cell counts using the Coulter counter technique for erythrocytes (red blood cells, RBC), platelets, total leukocytes (white blood cells; WBC) and differential counts for neutrophils, lymphocytes, monocytes and eosinophils. Quantitative determination of serum vitamin D (25-hydroxy cholecalciferol) concentration was done using an electrochemiluminescence binding assay (Elecsys[®] vitamin D total assay, Roche Diagnostics International Ltd., CH-6343 Rotkreuz, Switzerland) on a Cobas[®] e411 analyzer. Serum IgE levels were measured using a double-sandwich immunoassay for electro-chemiluminescent detection (Elecsys[®] IgE immunoassay, Roche Diagnostics International Ltd., CH-6343 Rotkreuz, Switzerland) on Elecsys[®] immunoassay analyzer. Serum parathyroid hormone levels (PTH) were estimated using a sandwich electrochemiluminescence immunoassay (Elecsys[®] PTH, Roche Diagnostics International Ltd., CH-6343 Rotkreuz, Switzerland) on a Cobas[®] e411 immunoassay analyzer. Serum calcium and phosphorus were also measured. A validated questionnaire was used to calculate the average daily sun exposure, which took into consideration factors including the time of day and duration of exposure, occupation, clothing and head gear [17]. Subjects were then grouped as those having 1) daily sun exposure < 1 hour, 2) daily sun exposure between 1 -2 hours and 3) daily sun exposure > 2 hours.

Data were analyzed in an anonymized form using the Statistical Package for Social Sciences (SPSS), version 23. Descriptive data were presented as frequencies and percentages. Group mean differences were assessed using the independent sample t-test, and correlations were assessed using Pearson's correlation.

Results

The participants were segregated into two groups: Group 1 (non-allergic healthy control subjects, n=41, mean age 44.37 ± 14.13 years) and Group 2 (allergic subjects, n=39, mean age 44.21 ± 15.30 years) with no age difference ($p=0.961$). Group 1 consisted of 24 males and 17 females, while Group 2 consisted

of 33 males and 6 females. Within the allergic subjects (Group 2), 9 (23%) people had ocular allergies, 13 (35%) had respiratory allergies, 3 (8%) had a food allergy, 4 (10%) had a dermal allergy and 10 (26%) had combined features of ocular and respiratory allergies (Figure 1). Among the 80 study participants, 51 (63.75%) had an average sun exposure of less than one hour per day. Thirty-two (78.4%) subjects in Group 1 and 19 (48.71%) in Group 2 had average daily sun exposure of less than one hour. Seven (17.07%) subjects in Group 1 and 12 (30.76%) in Group 2 had sun exposure between 1 to 2 hours per day. Only 1 (2.43%) subject in Group 1 and 8 (20.51%) in Group 2 had daily sun exposure of over 2 hours.

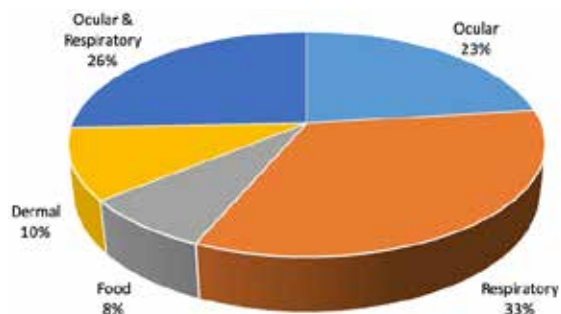


Figure 1. Distribution of subjects based on their allergic conditions.

Markedly high serum IgE levels were observed in allergic subjects compared to control subjects (Group 1, 87.13 IU/L ± 57.66 vs. Group 2, 1542.54 IU/L ± 1239.79; p=0.000)(Table 1). Significantly higher eosinophil count was seen in allergic subjects compared to control subjects (Group 1, 2.80% ± 1.83 vs. Group 2, 4.61% ± 4.19; p=0.014) (Table 2). No obvious difference was observed in any other parameter (Tables 1 and 2).

Table 1. Group comparison of serum IgE, vitamin D, PTH, calcium and phosphate

Parameter	Mean + St. Dev.		p-value
	Group 1 (Non-Allergic; n= 41)	Group 2 (Allergic; n =39)	
IgE (IU/mL)	87.13 ± 57.66	1542.54 ± 1239.79	0.000*
Vitamin D (ng/mL)	36.64 ± 21.05	40.13 ± 11.05	0.360
PTH (pg/mL)	32.57 ± 21.08	27.01 ± 17.55	0.205
Calcium (mg/dL)	9.49 ± 0.60	9.55 ± 0.74	0.698
Phosphate (mg/dL)	4.38 ± 0.83	4.61 ± 1.24	0.333

*Difference considered significant at p<0.05

Table 2. Group comparison of CBC parameters

Parameter	Mean + St. Dev.		p-value
	Group 1 (Non-Allergic; n= 41)	Group 2 (Allergic; n =39)	
Hemoglobin (g/dL)	13.48 ± 1.93	14.31 ± 1.86	0.053
RBC count (10 ¹² /L)	5.04 ± 0.70	5.29 ± 0.65	0.111
Hematocrit (%)	44.18 ± 6.45	46.73 ± 5.86	0.069
Platelet count (10 ⁹ /L)	201.51 ± 60.86	220.79 ± 62.97	0.168
WBC count (10 ⁹ /L)	7.72 ± 1.92	7.81 ± 2.01	0.83
Neutrophils (% WBC count)	55.39 ± 8.66	55.89 ± 9.41	0.803
Lymphocytes (% WBC count)	35.14 ± 7.91	34.12 ± 8.81	0.588
Monocytes (% WBC count)	6.85 ± 1.86	6.38 ± 2.02	0.284
Eosinophils (% WBC count)	2.80 ± 1.83	4.61 ± 4.19	0.014*

*Difference considered significant at p<0.05

A weak positive correlation was observed between serum vitamin D and IgE levels in Group 1, though it barely reached the level of significance (r= +0.309, p= 0.049) (Table 3, Figure 2). A significant negative correlation was seen between serum vitamin D and IgE levels in Group 2 (r= -0.374, p= 0.019) (Table 3, Figure 3).

Table 3. Correlation of Vitamin D and Serum Ig-E in Allergic & Non-Allergic Groups

Groups	r value	p-value
Group 1 (Non-allergic, n=41)	+0.309	0.049*
Group 2 (Allergic, n=39)	-0.374	0.019*

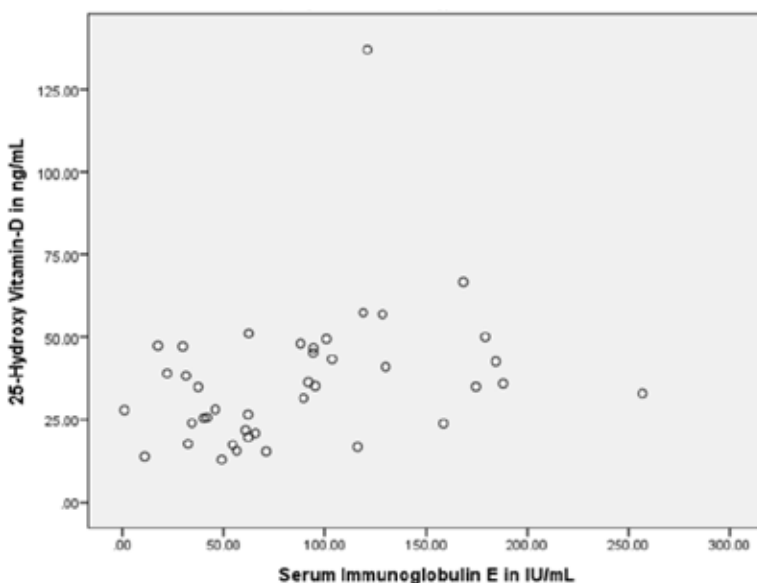


Figure 2. Scatter diagram of serum vitamin D and IgE in Group 1 (Non-allergic)

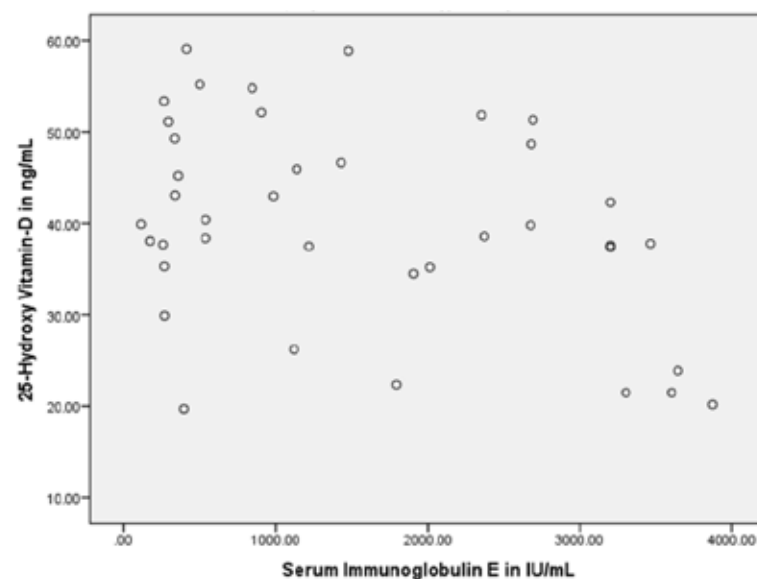


Figure 3. Scatter diagram of serum vitamin D and IgE in Group 2 (Allergic)

Discussion

The present study was carried out to assess serum IgE and vitamin D levels with other associated parameters in patients with allergies and to compare them with healthy non-allergic individuals. The results of the present study indicated considerably higher serum IgE levels and eosinophilia in persons with known allergies. No difference in circulating vitamin D levels was demonstrated between healthy non-allergic subjects and allergic subjects, suggesting that vitamin D status does not change in allergic conditions. However, serum vitamin D levels were found to be inversely correlated with serum IgE levels in allergic patients, reflecting the potential protective role of vitamin D against progression of allergy. Higher vitamin D levels in patients with allergic predisposition may have a role in mitigating the severity of the disease.

The present findings are in line with those reported in several other studies. In a study of patients with bronchial asthma, low vitamin D levels in the serum were associated with increased severity and poor disease control. Additionally, vitamin D levels were also shown to be associated with higher serum IgE levels and eosinophilia [5]. An observational case-control study by Dadaci et al. in patients with seasonal allergic conjunctivitis reported higher serum IgE levels [2]. A recent study by Ansari et al. showed significantly higher serum IgE levels in patients with allergic rhinitis [18]. Similarly, another study by Demir et al. on patients diagnosed with allergic rhinitis revealed higher serum IgE levels, and a significant negative correlation was reported between serum IgE and vitamin D levels in patients with allergic rhinitis [19]. A case-control study of young children with recurrent wheeze reported elevated serum IgE and eosinophil counts in patients compared with controls. An inverse correlation was also observed between serum vitamin D levels and disease severity [20].

Many preceding studies have shown serum vitamin D levels to be lower in patients with allergic conditions compared to age-matched non-allergic healthy individuals [2, 5, 18, 19, 21]. The findings from the current work did not demonstrate such a difference in serum vitamin D levels between allergic and healthy individuals, possibly because of the inclusion of multiple allergy groups, whereas the other studies targeted an exclusive allergic group including bronchial asthma, allergic conjunctivitis or allergic rhinitis. Moreover, several previous studies have shown sub-optimal vitamin D status in allergic as well as non-allergic groups but the mean vitamin D was optimal in our study population, including the allergic and non-allergic groups. In the present study, mean serum levels of other biochemical markers for skeletal health associated with vitamin D including PTH, calcium and phosphate were also within the normal range. Nevertheless, the existing data on circulating vitamin D levels in allergic patients compared to healthy subjects remain incongruous.

Our findings are in accordance with results from a study by Naghizadeh et al. in which no difference in serum vitamin D concentration was noted between allergic and non-allergic groups in a study of young adults [22]. The allergic group included patients diagnosed with allergic rhinitis, asthma and atopic dermatitis, which is similar to our mix of allergic patients. In line with our findings, serum IgE levels were also

shown to be elevated in allergic groups compared to the non-allergic group [22]. A genetic study by Manousaki et al. found no association of allergic conditions or raised IgE levels with alleles typically associated with reduced serum vitamin D levels [23]. However, the observation did not exclude association of serum vitamin D levels with allergic disorders or elevated IgE levels. Moreover, the study was conducted on a specific white European population and was not powered enough for general applicability of the results [23].

The present data showed that a higher number of patients with allergies had longer estimated sun exposure compared to healthy controls. Comparison of vitamin D levels between groups based on the duration of sun exposure could not be performed due to the discrepant distribution of subjects in each group. The role of sun exposure in allergic conditions needs to be evaluated since endogenous vitamin D synthesis occurs under the influence of ultraviolet rays from the sun, and adequacy of dietary vitamin D intake and sun exposure have been shown to be associated with reduction in respiratory allergies [17, 24]. Conversely, long sun exposure has also been associated with exacerbation of allergic symptoms [25]. The present work is limited by its relatively small sample size and distribution, which did not allow comparisons between different allergic groups. Moreover, the present study design did not permit intervention with vitamin D supplementation in allergic patients and their follow-up. Large scale studies with randomization and subset analysis are needed to elicit concrete clinical evidence on the role of vitamin D in allergic conditions.

Conclusion

The present study has brought forth an inverse relationship between serum vitamin D and IgE levels in the local population affected by various forms of allergies. The generated data suggest that vitamin D has a potentially beneficial role in ameliorating IgE-mediated hypersensitivity in patients with allergies. Estimation of serum levels of vitamin D in patients diagnosed with allergies may be contemplated as part of their clinical management. The present findings indicate a possible therapeutic function for supplementation of vitamin D in allergic disorders, but comprehensive future studies are needed for further exploration of this aspect in order to derive meaningful conclusions.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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